

Anti Hepatitis C Drugs

Presented to: Dr.Fiaz-ud-Din

Presented by: Hafiz Muhammad Zubair

Introduction

- **Hepatitis** (Hepatitides) is a medical condition defined by the inflammation of the liver caused by a viral infection and characterized by the presence of inflammatory cells in the tissue of the organ.
- The word commonly is from Greek “Hepato” meaning **Liver** and suffix “itis” meaning **Inflamma**.
- **Causes:**
 1. Genetic diseases
 2. Medications(OTC)
 3. Alcohol
 4. Hepatitis Viruses (A,B,C,D,E)

Hepatitis C Virus:

- is caused by single stranded RNA virus.
- Its size is 60nm and incubation period is 6 to 7 weeks.
- Can survive outside the body at room temperature on environmental surfaces for at least 16 hours but no longer than 4 days.
- Uses liver cells to create copies of itself, killing those cells in the process.
- Is an infectious form of hepatitis.

Factors	Hepatitis C
Source of Transmission	Blood Body fluids
Chronic Infection	Yes
Diagnostic Tests	Anti-HCV or anti-HDV, HCV RNA
Signs and symptoms	Similar to HBV, Less severe
Prevention and treatment	Blood donor Screening, Peginterferon, Ribavirin, Sofosbuvir

Transmission

1. Sharing needles, pipes , straws , filters or water for drug use.
2. Piercing or tattooing equipment used on someone else
3. Hygiene/grooming such as razors, nail clippers, and tooth brushes.
4. Unprotected sex
5. Reusing medical equipment that was not properly sterilized
6. It can also pass from mother to unborn child.

Goals of Therapy

Primary Goal:

- Eradicate HCV infection

Secondary Goal:

- Slow disease progression
- Improve histology
- Reduce risk of Hepatocellular Carcinoma
- Improve health related quality of life.

Prevention

- No vaccine for the prevention of HcV
- Never share needles
- Avoid direct exposure to blood or blood products
- Don't share personal care items
- Choose tattoo and piercing parlors carefully
- Practice safe sex
- Avoiding alcohol and drugs that can damage the liver, it may help slow the rate of progression of the disease.

Treatment of acute hepatitis:

- Treatment of acute hepatitis C include alpha and beta interferon monotherapy.
- It significantly decreases the number of patients that become chronic carriers.

Acute Hepatitis C	Treatment
Genotype 1,2,3,4	Interferon monotherapy
	Interferon + Ribavarin
	Peg-interferon Monotherapy
	Peginterferon + Ribavarin

Treatment of chronic hepatitis

- **Interferon:**

Given by shot usually 3 times a week

Dose: Interferon alpha 3 MIU TIW SC

Pegylated interferon: Long acting taken once a week

Drug	Form	Recommended treatment/regimen
Pegylated interferon alpha-2b (PEG-Intron)	Pen injection system	1.5 mcg per kg subcutaneously once weekly
Pegylated interferon alfa 2a (Pegasys)	Prefilled syringe	180 mcg subcutaneously once weekly

Combination therapy

- Interferon (standard or pegylated) taken with antiviral drug Ribavarin (Virazole) is the treatment of choice for chronic hepatitis C

Drug	Form	Regimen
Ribavarin (Rabetol) For viral genotype 1	Capsule	Weight 75kg or greater ;three 200mg capsules twice daily (total daily dose of 1200 mg)
		Weight less than 75kg;two 200mg capsules every morning and three 200mg capsules every evening (total daily dose of 1,000mg)
For genotype 2,3		All weight; two 200 mg capsules twice daily (total daily dose of 800 mg)

Is the treatment effective?

- **Interferon alone:**

10-15% chance of clearing the virus from the blood

- **Interferon and Ribavarin:**

Upto 40% chance of clearing the virus

- **Pegylated interferon alone:**

About the same as interferon & ribavirin 40%

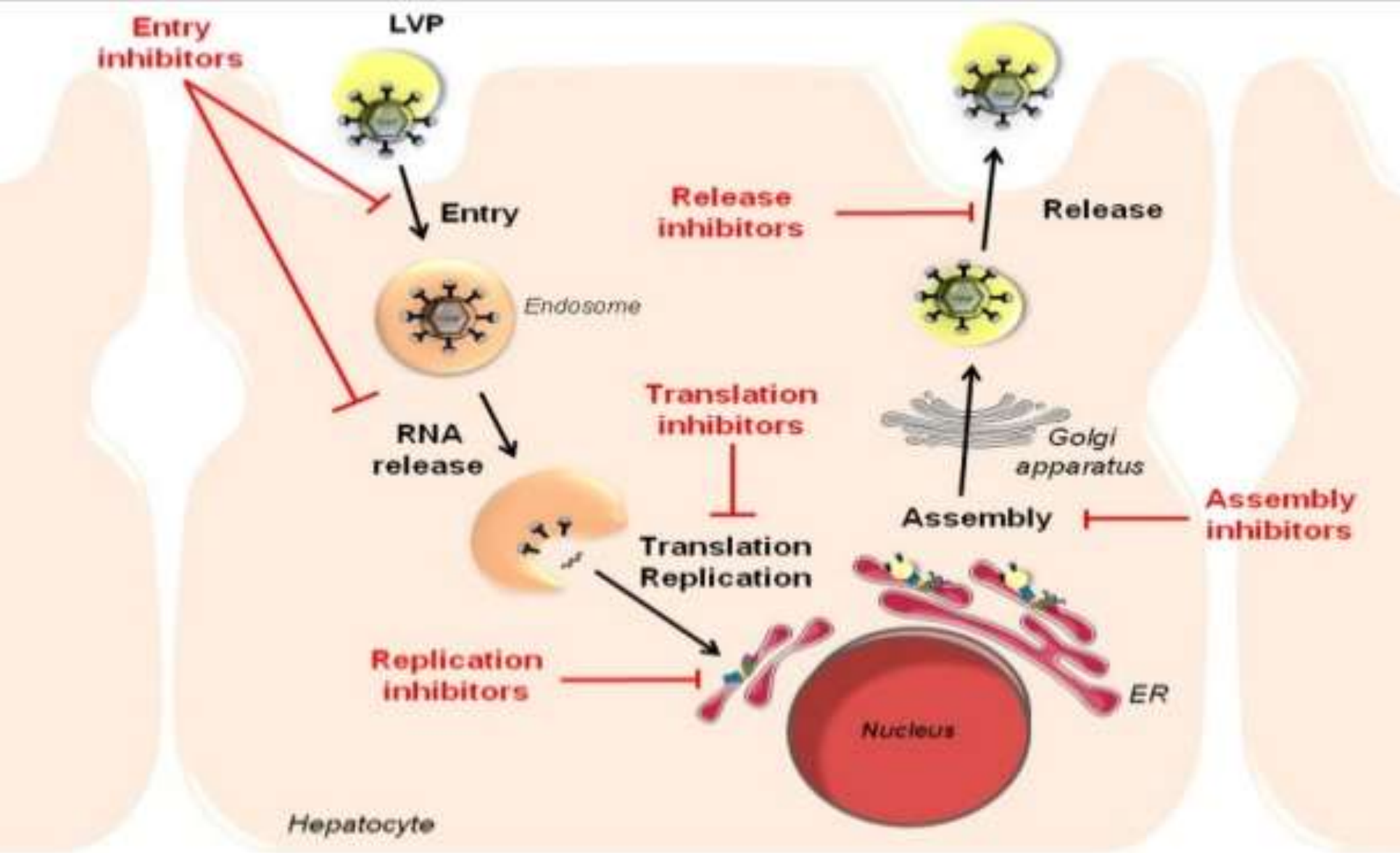
- **Pegylated interferon & Ribavarin:**

Upto 50% chance of clearing the virus

Interferons (IFNs) (Avonex)

- These are the proteins synthesized by the host cells in response to various inducers and in turn cause biochemical changes leading to antiviral state in cells.
- **Types:**
 1. Alpha
 2. Beta
 3. Gamma

Mechanism of action:



lipoviroparticle
(LVP)

Endoplasmic
reticulum (ER)

Therapeutic uses and adverse effects

Therapeutic uses:

1. Anti-virals
2. Anti-proliferative
3. Immuno-modulatory activity

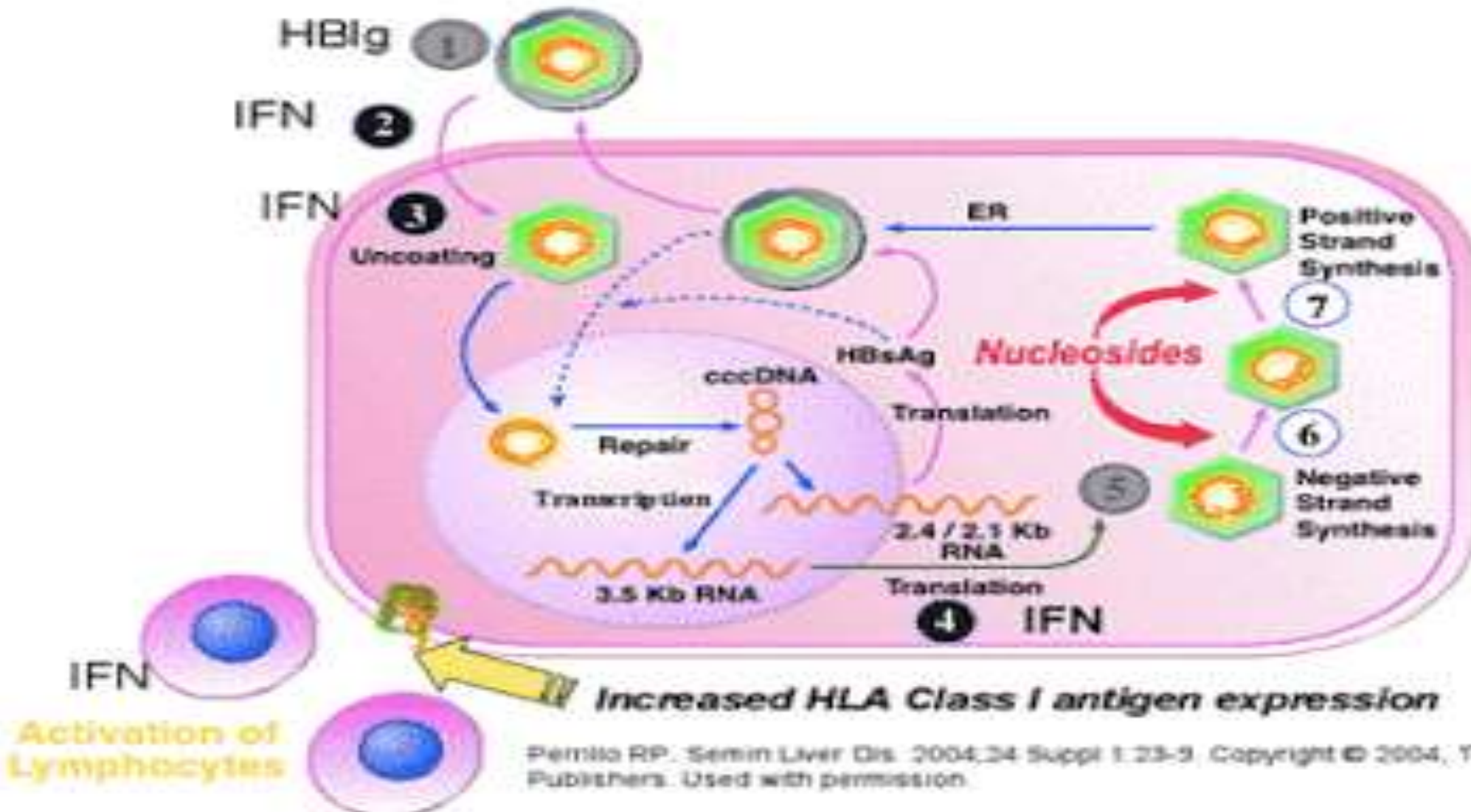
Adverse effects: Doses > 1 to 2 MU cause influenza like syndrome.

1. Fever
2. Myalgia, Anthralgia
3. Chills
4. Headache
5. diarrhea

Pegylated interferons (pegasays)

- HCV treatment improved again in 2001 with FDA approval of pegylated interferon.
- Attaching polyethylene glycol (PEG) molecule to interferon (a process called pegylation) keeps the drug in the blood stream longer and makes it more effective against HCV.
- **Types:**
 1. Peginterferon –alpha-2a
 2. Peginterferon –alpha -2b

Mechanism of action



Therapeutic uses & ADRs

Therapeutic uses:

1. Indicated for the treatment of patients with chronic hepatitis C who have compensated liver disease.

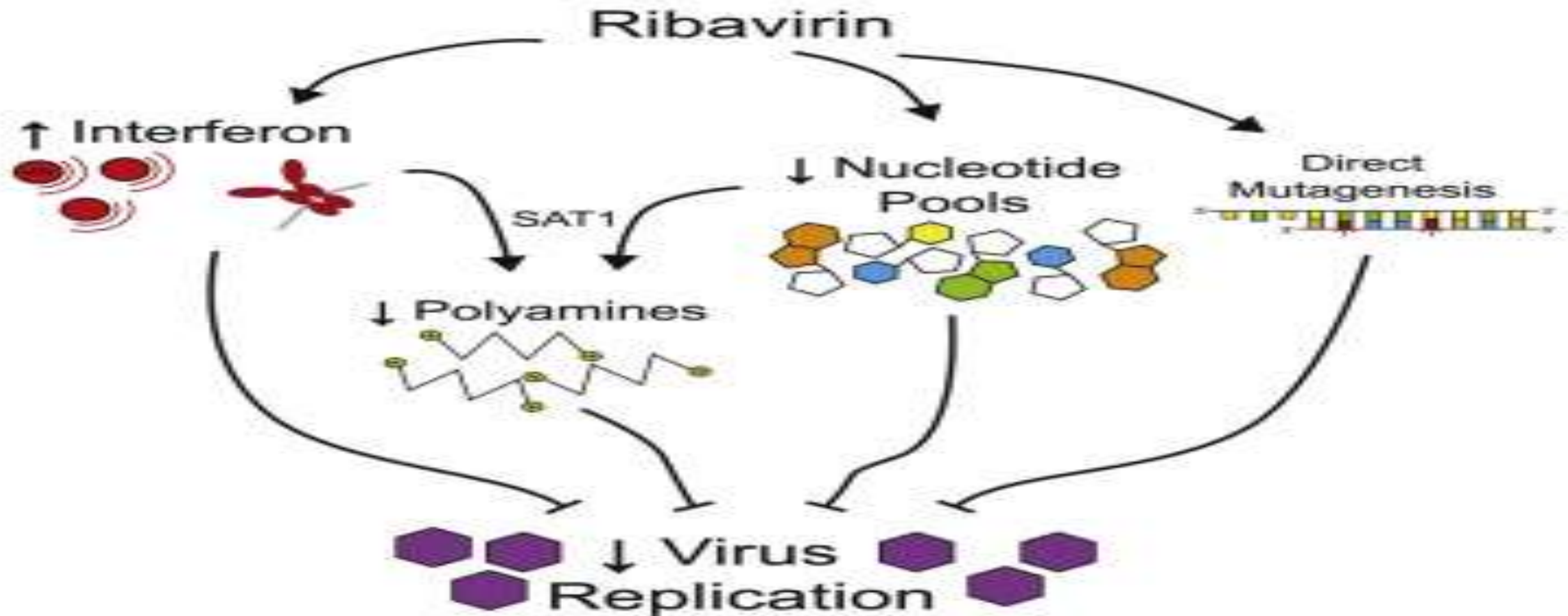
ADRs:

1. Retinopathy
2. Optic neuropathy
3. Ocular loss

Ribavarin (Virazole)

- It is an antiviral drug, a purine nucleoside analogue with a modified bases and D-Ribose sugar
- It inhibits the replication of wide range of RNA and DNA viruses.

Mechanism of action



Therapeutic uses and ADRs

- **Monotherapy:**

- For 6-12 months

- It decreases aminotransferases elevations to normal but does not effect HCV RNA level.

Adverse drug reactions:

1. Conjunctival irritation
2. Rash
3. Transient wheezing
4. Fatigue
5. depression

Older Direct acting antivirals (DAA)

- **Boceprevir and Telaprevir:**
- They are **Protease inhibitors**.
- Developed in May of 2011, they were the first drugs to act directly on the HCV virus.
- Increased the cure rate for HCV genotype 1 to 70%
- A treatment regime with boceprevir or telaprevir with Interferon and Ribavarin lasts **24-48 weeks**.

New Direct acting Antivirals:

➤ **Sofsbobuvir: (SOVALDI)**

- Sovaldi is hepatitis C virus nucleotide analog NS5B polymerase inhibitor among the second generation of protease inhibitors that directly attack the Hep C virus cell.
- Sofsbobuvir was approved by FDA on 6th December 2013.

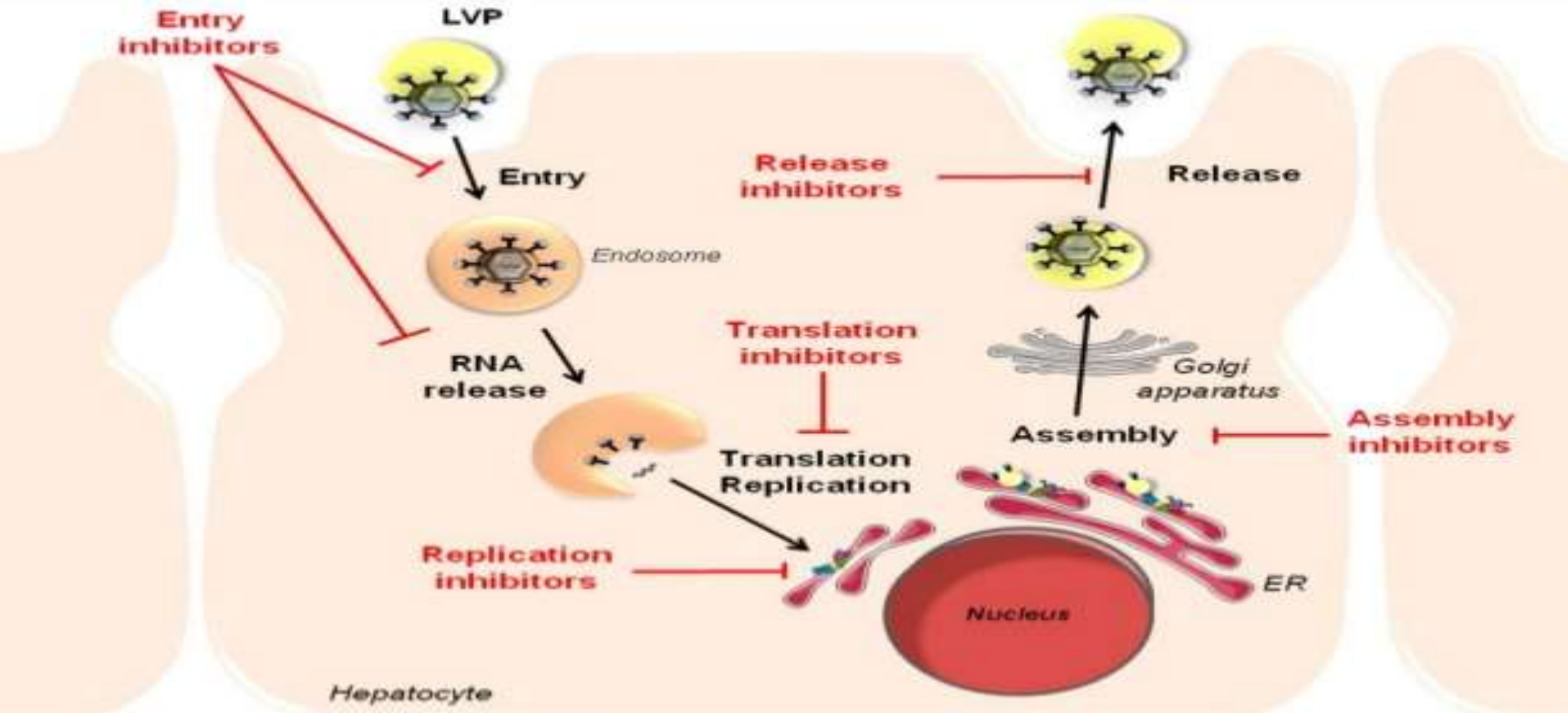
Dosage and administration:

- One 400mg tablet taken orally daily with or without food
- Should be use din combination with Ribavarin or in combination with Pegylated interferon and ribavirin for the treatment of HCV.
- Should be used in combination with Ribavarin in patients with hepatocellular carcinoma awaiting liver transplantation for upto 48 weeks or until liver transplantation, whichever occurs first.

Regimen:

Patient population	treatment	Duration
Genotype 1,4	Solvadi + Peg-interferon alpha+ Ribavarin	12 weeks
Genotype 2	Solvadi + Ribavarin	12 weeks
Genotype3	Solavdi + RIbavarin	24 weeks

Mechanism of action:



Therapeutic Uses and ADRs:

Therapeutic uses:

1. Indicated for treatment of genotype 1,2,3,or 4 chronic hepatitis C Virus (HCV).
2. It is the first drug that has demonstrated safety and efficacy to treat certain types of HCV infection without the need for co-administration of interferon

ADRs:

In combination with Ribavarin

- Fatigue, headache

In combination with peg-interferon alpha:

- Insomnia, anemia and fatigue

What medications to avoid?

- Acetaminophen
- Ibuprofen
- Iron supplements
- Amidarone
- P-gp inducers

Where HCV therapy stands now?

- Interferon is gone
- SVR in >95% of pts
- “Difficult to cure” population is no longer difficult
- ✓ HIV co infection Cirrhosis
- ✓ Persons who inject drugs (PWID)
- ✓ Renal failure and kidney transplant
- ✓ Liver transplant old age
- Emergent issues and controversies:
 - ✓ HBV reactivation
 - ✓ HCC recurrence after DAA therapy

Thank you

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